

WHAT IS CLAIMED IS:

1. A method of predicting whether a subject will be susceptible to undesirable toxicity resulting from treatment with an anti-proliferative therapy, said method comprising:
 - (a) obtaining an expression profile for any gene from Table3 for a response to said anti-proliferative therapy in a sample from said subject; and
 - (b) comparing said obtained expression profile to a reference expression profile to predict whether said subject is susceptible to undesirable toxicity.
2. The method according to Claim 1, wherein said anti-proliferative therapy comprises administration of ionizing radiation.
3. The method according to Claim 1, wherein said anti-proliferative therapy comprises administration of a chemotherapeutic agent that results in DNA damage.
4. The method according to Claim 3, wherein said DNA damage comprises double-stranded breaks in DNA.
5. A method of determining whether a subject is susceptible to undesirable toxicity resulting from treatment with radiation therapy, said method comprising:
 - (a) obtaining an expression profile for the response to radiation for a sample for any gene from Table3 from said subject; and
 - (b) comparing said obtained expression profile to a reference expression profile to determine whether said subject is susceptible to undesirable radiation toxicity.
6. The method according to Claim 5, wherein expression profile is a transcriptional profile.
7. The method according to Claim 5, wherein said expression profile comprises at least 10 sequences from Table3.
8. The method according to Claim 5, wherein said expression profile comprises at least 50 sequences from Table 3.

9. The method according to Claim 5, wherein said undesirable toxicity is at least a grade 2 toxicity.

10. A method of determining whether a subject is susceptible to undesirable toxicity resulting from treatment with administration of a chemotherapeutic agent that induces double-stranded breaks in DNA, said method comprising:

(a) obtaining an expression profile for the response to said chemotherapeutic agent for a sample for any gene from Table 3 from said subject; and

(b) comparing said obtained expression profile to a reference expression profile to determine whether said subject is susceptible to undesirable toxicity.

11. A method of predicting whether a subject will be susceptible to undesirable toxicity resulting from treatment with radiation therapy, said method comprising:

(a) obtaining an expression profile for the response to radiation for a sample for any gene from Table 3 from said subject; and

(b) comparing said obtained expression profile to a reference expression profile to determine the probability that said subject is susceptible to undesirable radiation toxicity.

12. The method according to Claim 11, wherein expression profile is a transcriptional profile.

13. The method according to Claim 11, wherein said expression profile comprises at least 10 sequences from Table 3.

14. The method according to Claim 11, wherein said expression profile comprises at least 50 sequences from Table 3.

15. The method according to Claim 11, wherein said undesirable toxicity is at least a grade 2 toxicity.

16. A method of predicting whether a subject will be susceptible to undesirable toxicity resulting from treatment with administration of a chemotherapeutic agent that induces double-stranded breaks in DNA, said method comprising:

(a) obtaining an expression profile for the response to said chemotherapeutic agent for a sample for any gene from Table 3 from said subject; and

(b) comparing said obtained expression profile to a reference expression profile to determine the probability that said subject is susceptible to undesirable toxicity.

17. A method of determining the suitability of a patient for radiation therapy, the method comprising:

predicting whether a subject will be susceptible to undesirable toxicity resulting from treatment with radiation therapy, said method comprising:

(a) obtaining an expression profile for the response to radiation for a sample for any gene from Table 3 from said subject; and

(b) comparing said obtained expression profile to a reference expression profile to determine the probability that said patient is susceptible to undesirable radiation toxicity;

wherein a patient that is predicted to have a high probability of undesirable radiation toxicity is less suitable for radiation therapy.

18. The method according to Claim 17, wherein expression profile is a transcriptional profile.

19. The method according to Claim 17, wherein said expression profile comprises at least 10 sequences from Table 3.

20. The method according to Claim 17, wherein said expression profile comprises at least 50 sequences from Table 3.

21. The method according to Claim 17, wherein said undesirable toxicity is at least a grade 2 toxicity.

22. A method of determining the suitability of a patient for treatment with an anti-proliferative chemotherapeutic agent that induces double-stranded breaks in DNA, the method comprising:

predicting whether a subject will be susceptible to undesirable toxicity resulting from treatment with said chemotherapeutic agent, said method comprising:

(a) obtaining an expression profile for the response to said chemotherapeutic agent for a sample for any gene from Table3 from said subject; and

(b) comparing said obtained expression profile to a reference expression profile to determine the probability that said patient is susceptible to undesirable toxicity;

wherein a patient that is predicted to have a high probability of undesirable toxicity is less suitable for said treatment with an anti-proliferative chemotherapeutic agent.

23. A method of optimizing anti-proliferative therapy for a patient, the method comprising:

(a) obtaining an expression profile for the response to said anti-proliferative therapy for a sample for any gene from Table3 from said subject; and

(b) comparing said obtained expression profile to a reference expression profile to determine the probability that said patient is susceptible to undesirable toxicity;

wherein a dose of said anti-proliferative therapy is selected to minimize to undesirable toxicity, while providing for effective anti-proliferative activity.

24. The method according to Claim 23, further comprising obtaining an expression profile for a response to one or more additional anti-proliferative therapies;

comparing said expression profiles to determine which therapy minimizes undesirable toxicity while providing for effective anti-proliferative activity.

25. The method according to Claim 23, further comprising obtaining an expression profile for the response to said anti-proliferative therapy for (i) a normal cell sample for any gene from Table3 from said subject and (ii) a tumor cell sample for any gene from Table3 from said subject;

comparing said expression profiles from said normal cell and said tumor cell to determine which therapy minimizes undesirable toxicity while providing for effective anti-proliferative activity.

26. A method of obtaining an expression profile for the transcriptional response to radiation, the method comprising:

exposing a cell sample from an individual to radiation;

extracting mRNA from said cell;

quantitating the level of mRNA corresponding to a sequence in Table 3;
comparing said level of mRNA to the level of said mRNA present in a cell sample from said individual not exposed to radiation.

27. The method according to Claim 26, wherein said exposing to radiation comprises exposes said cell to a dose of ionizing radiation of from about 2 to about 10 Gy.

28. The method according to Claim 27, wherein said mRNA is extracted after at least about 2 and not more than about 24 hours following said exposure.

29. The method according to Claim 27, further comprising exposing a cell sample from said individual to ultraviolet radiation at a dose of at least about 5 J/m² and not more than about 50 J/m².

30. The method according to Claim 29, wherein said mRNA is extracted after at least about 4 and not more than about 72 hours following said exposure.

31. The method according to Claim 26, wherein said comparing step comprises a nearest shrunken centroid analysis step.

32. A method of obtaining an expression profile for the transcriptional response in a phenotype of interest, the method comprising:

exposing a cell sample from an individual to said anti-proliferative therapy;
extracting mRNA from said cell;
quantitating the level of mRNA corresponding to a sequence of interest;
comparing by nearest shrunken centroid analysis said level of mRNA to the level of said mRNA present in a cell sample from said individual not exposed to said anti-proliferative therapy.

33. The method according to Claim 32, wherein said phenotype of interest comprises anti-proliferative therapy.

34. A kit for determining susceptibility to undesirable toxicity, the kit comprising:

a set of primers specific for at least 10 genes as set forth in Table 3; and instructions for use.

35. The kit according to Claim 34, further comprising a set of primers specific for at least 25 sequences set forth in Table 3.

36. The kit according to Claim 34, further comprising a set of primers specific for at least 50 sequences set forth in Table 3.

37. The kit according to Claim 34, further comprising a software package for statistical analysis of expression profiles.

38. A kit for determining susceptibility to undesirable toxicity, the kit comprising:
a microarray comprising probes specific for at least 10 genes as set forth in Table 3;
and instructions for use.

39. The kit according to Claim 38, further comprising probes specific for at least 25 sequences set forth in Table 3.

40. The kit according to Claim 38, further comprising probes specific for at least 50 sequences set forth in Table 3.

41. The kit according to Claim 38, further comprising a software package for statistical analysis of expression profiles.

42. A method for determining a set of sequences whose expression is predictive of a phenotype of interest, the method comprising:

obtaining an expression profile for a set of candidate sequences from a cohort group having said phenotype of interest and from a control group;

subjecting said expression profiles to heterogeneity associated transformation;

analyzing transformed or untransformed expression profile data by nearest shrunken centroids; and

calculating the probability that a specific sequence is predictive of said phenotype of

interest.

43. The method according to Claim 42, wherein said sequence is a nucleotide sequence expressed in a target cell.

44. The method according to Claim 42, wherein said sequence is a protein sequence expressed in a target cell.

45. The method according to Claim 42, wherein said sequence is a protein sequence post-translationally modified in a target cell.

46. The method according to Claim 42, wherein said obtaining an expression profile for the transcriptional response to radiation comprises:

exposing a cell sample from an individual to stimulus;

extracting mRNA or protein from said cell;

quantitating the level of mRNA or protein;

comparing said level of mRNA or protein to the level present in a cell sample from said individual not exposed to said stimulus.